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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

TON, THAIAN N

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 09/12/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/654,293

Applicant(s)

CHRISTMANN ET AL.

Examiner

Thaian N. Ton

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 11, 14-22 and 24-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 11, 14-22 and 24-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' Amendment, filed June 11, 2002, Paper No. 9, has been entered. Claims 1, 5, 11, 14, 19, 21 have been amended. Claims 7-10, 12, 13, 23 have been cancelled. Claims 28-33 have been added.

Claims 1-6, 11, 14-22, 24-33 are pending and under current examination.

Any rejection made of record in the prior Office action, mailed 12/05/2001, Paper No. 6, and not made of record in the instant Office action, has been withdrawn in view of Applicants' arguments and/or amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11, 14-22, 24-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is directed to cloned avian, methods of producing cloned avians, methods of producing reconstructed avian zygotes or oocytes, and methods of producing a protein from the cloned avians.

Applicants' arguments and amendments to the claims have been carefully considered; however, they are not found persuasive. Applicants state they specifically teach the use of nuclear transfer via two photon laser scanning microscopy [TPLSM] for nuclear transfer in avian. Applicants state that ovum transfer and *ex ovo* culture is taught by the instant specification [see pp. 11-12 of the Response]. Applicants argue that by employing TPLSM, Applicants have overcome a significant hurdle in avian nuclear transfer, i.e., the visualization of the early avian egg, and thus, visualization of target structures in the early avian embryo. Applicants state that they have successfully employed TPLSM for ablation of the nuclear structures and this technique is less invasive than microsurgery [see pp. 12-13 of the Response]. Applicants argue that they describe a method of producing a cloned animal via nuclear transfer in combination with ovum transfer, and they provide additional guidance through illustration via detailed examples, wherein Applicants elaborate on the preparation of the recipient cytoplasm, preparation of the reconstructed zygote, and ovum transfer into hens. Applicants argue that one of skill in the art would easily be able to follow Applicants' teachings in order to clone avian as described in the instant invention [see p. 13 of the Response]. Applicants submit that the nature of the instant invention is complex and may require some experimentation, but the complexity of the invention does not prevent one skilled in the art from practicing what is taught. Applicants argue that the combination of Applicants' teachings and the state of the

art of nuclear transfer would enable the skilled artisan to produce the cloned avian of the instant invention. Applicants argue that their teachings alone provide explicit guidance of how to clone avian, and in particular chickens, and that the courts have repeatedly held that a "patent need not teach, and preferably omits what is well-known in the art." [See p. 14 of the Response].

In response, it is noted that the rejection of the claimed invention with regards to enablement, is dependent on the state of the art. For reasons advanced in the prior Office action [pp. 3-5], it is maintained that the state of the art of nuclear transfer is not predictable with regard to the production of cloned animals, and in the instant case, cloned birds. In particular, the specification does not provide sufficient teachings or guidance to show that cloned avian could be produced the claimed method of nuclear transfer, as the specification only putatively describes how ova prepared by nuclear transfer could be transferred into recipient hens which could then lay the eggs [Example 4]. As stated in the prior Office action, numerous factors affect the cloning of animals, and the state of the art of nuclear transfer is such that one of skill in the art could not predictably produce cloned or transgenic avian without specific teachings provided by the specification [see pp. 6-7].

Furthermore, certain embodiments of the claimed invention are directed to producing reconstructed avian zygotes or oocytes [see claims 1-6, 11, for example]; however, the method steps of the claims do not enable the claimed invention

because the claims do not include an activation step. It is well-known in the nuclear transfer art that activation of the resulting nuclear transfer unit must take place in order to effect further development; however, the claims do not provide such steps. Dinnyés *et al.* [Cloning & Stem Cells, 4:81-90, 2002] report on the state of the art of somatic cell nuclear transfer state that, "NT is a complex procedure and each step effects the overall efficiency. The unpredictability of the technology due to biological variation of the recipient oocytes and the donor cells is difficult to control. Therefore, standardization of the steps is important in order to obtain consistent results." [See p. 83, 1st column, 2nd full paragraph]. With particular regard to the importance of the activation of oocytes, Dinnyés *et al.* state that, "In NT, the lack of sperm-induced fertilization steps necessitate the application of an artificial activation in order to trigger further development." [See p. 83, 2nd column, last paragraph]. Furthermore, the claimed reconstructed avian zygotes or oocytes are not enabling because, although the specification provides guidance with regard to producing them, the specification does not provide specific teachings or guidance as to how to use the claimed reconstructed avian zygotes or oocytes, except for the generation of cloned or transgenic avian. As such, the specification does not teach how to make and use the claimed reconstructed zygotes or oocytes.

Applicants argue that, with regard to the state of the art of transgenesis, there would not be undue experimentation required to practice the claimed invention. In particular, Applicants quote Westhusin *et al.* "Work involving other

species is currently ongoing and information gathered to date suggests a wide variety of different animal species can be cloned by nuclear transplantation.” Applicants argue that this supports that the skilled artisan does not agree with the Examiner.

In response, it is noted that the quotation provided by Applicants’ further supports what the Examiner has stated *supra*, in particular, that the state of the nuclear transfer art, at present, is not predictable with respect to any particular species because, as stated in the prior Office Action on p. 3, Westhusin *et al.* state that, “While the basic approach involving nuclear transfer may be similar, the specific materials and methods utilized for cloning one species of animal do not automatically apply across different species.” As such, the state of the art supports that nuclear transfer protocol have not been optimized for all species, and without specific teachings provided by the specification to overcome the unpredictabilities of the nuclear transfer art, it would have required undue experimentation for the skilled artisan to make and/or use the claimed reconstructed avian zygote, oocytes, or cloned or transgenic avian.

Additionally, in the prior Office action, the Examiner has provided references with regard to the unpredictability in the state of the art of transgenesis [see pp. 6-7 of the prior Office action]. As such, it is reiterated that the expression of the transgene and the effect of transgene expression on the phenotype of the transgenic animal depends on the particular gene construct used, to an unpredictable extent.

Art Unit: 1632

With the lack of working examples provided by the specification, as well as the unpredictability in the art, one of ordinary skill in the art would have been required to engage in undue experimentation in order to make and use the claimed transgenic avian.

Therefore, in view of the quantity of experimentation necessary to determine the parameters for nuclear transfer for the production of reconstructed avian zygotes, oocytes or cloned or transgenic avian, the lack of direction or working examples provided by the specification for the production of cloned or transgenic avian, as well as the unpredictable state of the art of nuclear transfer and transgenics, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25, 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25, as written, is unclear. The claim recites that the hard-shell egg contains "less than the normal complement" of endogenous proteins found in the

egg. However, the metes and bounds of the term "normal complement" are not defined by the claim.

Claim 27 recites "An embryo" of claim 26. This renders the claim unclear because there is only one embryo recited in claim 27. It is suggested that the claim be written to state, "The embryo".

Claims 28 and 30 recite limitation "the process of claim 1" in part (i) of the claims. There is insufficient antecedent basis for this limitation in the claim. Claim 29 depends from claim 28, claim 31 depends from claim 30.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang *et al.* [Cell Biology International, 21:495-499, 1997].

Claim 26 is directed to a reconstituted avian embryo prepared by transferring the nucleus of a donor cell into a suitable recipient cell. Claim 27 is directed to the embryo of claim 26 in which the donor cell is quiescent. The claims are product by process claims. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical

processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In *re Best*, *Bolton*, and *Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

As such, the claims are properly interpreted as an avian embryo. *Chang et al.* teach the injection of cultured PGCs into recipient embryos obtained from the Korean native ogol chicken [see p. 496, 1st column].

Accordingly, *Chang et al.* anticipate the claimed invention.

Art Unit: 1632

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Patsy Zimmerman, Patent Analyst, at (703) 305-2758. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703)872-9306.

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